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DEC 14 2006

Application No. 10/790,069  
Amendment filed on December 14, 2006  
Reply to Office Action of September 15, 2006

Docket No.: 2410-0184P

**REMARKS**

Claims 1-7 and 19-24 are now present in this application.

The specification, abstract, and claims 1-7 and 19-24 have been amended, and claims 8-18 have been cancelled without prejudice or disclaimer. Reconsideration of the application, as amended, is respectfully requested.

**Objections to the Claims**

The claims stand objected to for certain informalities. In view of the foregoing amendments, it is respectfully submitted that these informalities have been addressed. Reconsideration and withdrawal of any objection to the claims are respectfully requested.

**Rejection under 35 USC 112**

Claims 1-24 stand rejected under 35 USC 112, second paragraph. This rejection is respectfully traversed.

The Examiner has noted certain phrases which are alleged to render the claims indefinite.

For example, the Examiner has indicated that claim 1 is unclear as to the steps of precipitation and separation. Accordingly, claim 1 has been amended to recite that the process includes the steps of using alcohol for precipitation of a concentrate from the fermentation broth; mixing alcohol with the concentrate to form a sediment; dissolving the sediment using distilled water to form an initial impure acarbose solution; and using a strong cation exchange chromatography and an immobilized enzyme affinity chromatography for purification of the acarbose-containing fermentation broth.

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The Examiner has also asserted that it is unclear how sodium chloride or ammonia solutions are used to remove impurities. Accordingly, the claims have been revised to clarify that a sodium chloride solution is used to wash an impurity from the resin and that an ammonia solution is used to elute further impurities from the resin.

The Examiner has also asserted that the use of the phrase "solved" or "solving" has rendered certain other claims indefinite. It is respectfully submitted that these typographical errors have been corrected, so as to be clear that the various powders and/or resins are being dissolved.

With regard to the remaining claim rejections, it is noted that, in view of the foregoing amendments, all claims should particularly point out and distinctly claim the subject matter of the instant invention. Reconsideration and withdrawal of the 35 USC 112, second paragraph rejection are respectfully requested.

Rejection under 35 USC 103

Claims 1-7 stand rejected under 35 USC 103 as being unpatentable over Hong et al., U.S. Patent 6,649,755, in view of Crueger et al., U.S. Patent 5,989,882. This rejection is respectfully traversed.

Claims 8-18 stand rejected under 35 USC 103 as being unpatentable over Hong et al. in view of Lawton et al., WO 99/07720. This rejection is respectfully traversed.

Claims 19-24 stand rejected under 35 USC 103 as being unpatentable over Hong et al. in view of Crueger et al. This rejection is respectfully traversed.

Independent Claim 1

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The present application sets forth a process in which alcohol is added to a fermentation broth to create a solution, which is then centrifuged and the concentrate removed therefrom. The concentrate is then added into a separate alcohol solution to form a sediment. The sediment is then removed therefrom, and dissolved using water to produce an impure acarbose solution. The impure acarbose solution is blended with a strong cation exchange resin to produce a resin, which is rinsed with sodium chloride and ammonia to remove impurities. The rinsed resin is then eluted with ammonia, and precipitated with alcohol, to produce acarbose powder with increased purity. The acarbose powder is then pH-adjusted and washed, and alcohol is used again to produce a concentrated sediment having high purity.

Hong et al., however, sets forth in column 3, lines 34-42, that "due to cation materials other than acarbose present in a filtrate obtained by filtration of mycelium from a fermentation broth, the adsorption of acarbose to a cation exchanger does not easily occur." Accordingly, Hong et al. teaches away from the present application, as instead of pursuing the use of a fermentation broth and ion exchangers, Hong et al. utilizes a synthetic resin and/or other *adsorbants* "to remove coloring materials and impurities other than acarbose and analogues thereof in an acarbose solution" (column 3, lines 40-42). The synthetic adsorbant is then washed, and the acarbose is eluted from the synthetic adsorbant using organic solvents (column 3, lines 61-64). The eluate is then "passed through an anion exchanger at a high flow rate to be decolorized and neutralized" (column 3, lines 64-66), "contacted with a monodispersed, strong acid cation exchanger" (column 4, lines 4-5) and finally "chromatographed with a diluted hydrochloric acid to remove the remaining" impurities (column 4, lines 14-17).

Accordingly, the Hong et al. differs from the present application in several key ways:

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1) The present application utilizes an absorbant resin (i.e., the acarbose molecules are moved into the bulk of the porous resin), whereas Hong et al. utilizes an adsorbant resin (i.e., the impure molecules stick to the surface of the resin). This should be clear in that, in the present application, the acarbose is repeatedly purified and concentrated by forming and resolubizing various sediments. In Hong et al., the acarbose is eluted (extracted) off of the resin, and the elute (liquid solution) is then purified and concentrated.

2) Although both the present application and Hong et al. teach the use of alcohols, the present application utilizes alcohol to form the initial concentrate from the fermentation broth, and again with the concentrate to form a sediment. That sediment is used to produce the initial impure acarbose solution. Alcohol is then mixed with the acarbose-absorbed resin in a later step, to remove impurities therefrom, etc. Accordingly, the alcohols of the present application are utilized to form precipitates and to remove impurities. In Hong et al., however, alcohols are used to elute the adsorbed acarbose from the resin.

Independent claim 1 of the present application sets forth:

1. A purification process for manufacturing a highly pure acarbose from an acarbose-containing fermentation broth, comprising the steps of:
  - using alcohol for precipitation of a concentrate from the fermentation broth;
  - mixing alcohol with the concentrate to form a sediment;
  - dissolving the sediment using distilled water to form an initial impure acarbose solution;
  - using a strong cation exchange chromatography and an immobilized enzyme affinity chromatography for purification of the acarbose-containing fermentation broth.

As set forth above, Hong et al. fails to teach or suggest "using alcohol for precipitation of a concentrate from the fermentation broth" or "mixing alcohol with the concentrate to form a

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sediment," as are set forth in independent claim 1. Although the Examiner asserts that Hong et al. discloses that acidic or basic aqueous solutions (such as a basic ammonia solution) are used as eluates, it is respectfully submitted that Hong et al. teaches the use of these aqueous solutions to elute adsorbed materials from nonspecific adsorptive resins to form an eluted solution containing the desired acarbose. The eluted solution is then neutralized, concentrated, precipitated, dissolved, and chromatographed, etc. (column 1, lines 43-54). This is unlike the present application, in which the various alcohols are used to form precipitates and remove impurities, as the resin of the present application has strong absorbance of acarbose, whereas the resin Hong et al. merely adsorbs acarbose. The secondary reference to Crueger fails to overcome the above-noted deficiencies.

In view of the foregoing amendments and remarks, it is respectfully submitted that Hong et al. and Crueger et al., either alone or in combination, fail to teach or suggest the process of independent claim 1 and its dependent claims. Reconsideration and withdrawal of this portion of the 35 USC 103 rejections are respectfully requested.

#### Independent Claim 8

Without conceding the appropriateness of the Examiner's rejections, but simply to expedite prosecution of this application, it is noted that claims 8-18 have been cancelled, thereby rendering this portion of the rejection moot.

#### Independent Claim 19

Independent claim 19 of the present application sets forth:

19. A purification process for manufacturing a highly pure acarbose, comprising the steps of:  
dissolving an acarbose powder having a purity of 83%~87% with distilled water, to form a solution;

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adjusting the pH value of the solution;  
 passing the solution through an  $\alpha$ -amyloglucosidase column;  
 washing the  $\alpha$ -amyloglucosidase column by using a volume of deionized water equal to twice the volume of the  $\alpha$ -amyloglucosidase column;  
 eluting acarbose fragments from the  $\alpha$ -amyloglucosidase column using distilled water;  
 concentrating the acarbose-containing fragments to be a volume of impure acarbose by a concentrating system; and  
 precipitating the impure acarbose to obtain a highly pure acarbose.

The Examiner confirms that Hong et al. fails to teach or suggest the use of immobilized enzyme affinity chromatography and instead relies on Crueger et al. to teach this feature.

First, it is noted that in the present application, the acarbose is purified by dissolving an acarbose powder in distilled water to form a solution, and then passing the solution through an  $\alpha$ -amyloglucosidase column. As discussed in Example 3, step 302 of the present application, the solution is passed through a strong cation exchange resin column, 8×50 cm, containing AMBERJET 1200 H resin (Rohm and Hass Company), and the strong cation exchange resin in the column is washed with deionized water until the absorbance of the strong cation exchange resin is zero or steady. The acarbose is therefore directly isolated from the solution based on the strong affinity between the acarbose and the  $\alpha$ -amyloglucosidase column.

In Crueger et al., the acarbose is processed in two steps. First, the amount of acarbose in the solution is increased, and the acarbose is subsequently purified. These steps are summarized in the following equation:



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It is respectfully submitted that the ATase of Crueger et al. is different from the  $\alpha$ -amyloglucosidase of the present application. In particular, ATase utilizes acarbose and its analog as a substrate. ATase also requires additional carbohydrates, such as glucose, maltose, maltooligosaccharides and other sugars, to complete the first transitional stage, and requires maltose to complete the second transitional stage. ATase transfers acarbose and its analog to a particular acarbose analog, such as Acarviosyl-starch, which is then transferred to acarbose. The  $\alpha$ -amyloglucosidase of the present application, however, simply absorbs the acarbose in a solution when the purity is around 85%. The acarbose can then be further isolated and purified using distilled water. Accordingly, the  $\alpha$ -amyloglucosidase of the present application does not require a substrate. The secondary reference to Crueger et al. therefore fails to overcome the above-noted deficiencies of Hong et al.

In view of the foregoing amendments and remarks, it is respectfully submitted that Hong et al. and Crueger et al., either alone or in combination, fail to teach or suggest the process of independent claim 19 and its dependent claims. Accordingly, reconsideration and withdrawal of this portion of the 35 USC 103 rejection are respectfully requested.

#### Conclusion

Favorable reconsideration and an early Notice of Allowance are earnestly solicited.

In the event that any outstanding matters remain in this application, the Examiner is invited to contact the undersigned at (703) 205-8000 in the Washington, D.C. area.

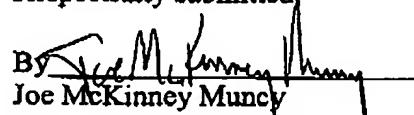
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If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: December 14, 2006

Respectfully submitted,

By   
Joe McKinney Muncy  
Registration No.: 32,334  
BIRCH, STEWART, KOLASCH & BIRCH, LLP  
8110 Gatehouse Road  
Suite 100 East  
P.O. Box 747  
Falls Church, Virginia 22040-0747  
(703) 205-8000  
Attorney for Applicant